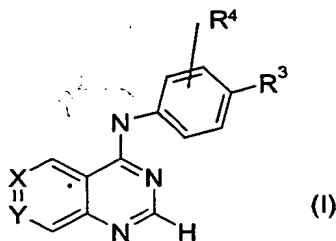


We claim:

1. A compound of formula (I)



or a salt or solvate thereof, or physiologically functional derivative thereof;

wherein

X is CR<sup>1</sup> and Y is N;  
or X is N and Y is CR<sup>1</sup>;  
or X is CR<sup>1</sup> and Y is CR<sup>2</sup>;  
or X is CR<sup>2</sup> and Y is CR<sup>1</sup>;

R<sup>1</sup> represents a group R<sup>5</sup>SO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Z-(CH<sub>2</sub>)<sub>p</sub>-Ar-, wherein Ar is selected from phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkoxy groups; Z represents O, S, NH or NR<sup>6</sup>; p is 1, 2, 3 or 4;

R<sup>5</sup> is C<sub>1-6</sub> alkyl optionally substituted by one or more R<sup>8</sup> groups; or

R<sup>5</sup> is C<sub>1-6</sub> alkyl substituted by a 5 to 10-membered heterocyclic group or a 3 to 10-membered carbocyclic group, each of which may be optionally substituted by one or more R<sup>8</sup> groups; or

R<sup>5</sup> is selected from the group consisting of a 5 to 10-membered heterocyclic group or a 3 to 10-membered carbocyclic group, each of which may be optionally substituted by one or more R<sup>8</sup> groups;

each  $R^8$  is independently selected from halo, hydroxy,  $C_{1-4}$  alkoxy, nitrile,  $NH_2$  or  $NR^6R^7$ ;

$R^6$  is  $C_{1-4}$  alkyl,  $C_{1-4}$  alkoxy- $C_{1-4}$  alkyl, hydroxy $C_{1-4}$  alkyl,  $CF_3C(O)$  or  $CH_3C(O)$ ;

$R^7$  is hydrogen or  $R^6$ ;

$R^2$  is selected from hydrogen, halo, hydroxy,  $C_{1-4}$  alkyl and  $C_{1-4}$  alkoxy;

$R^3$  is selected from pyridylmethoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy;

$R^4$  is selected from hydrogen, halogen,  $C_{1-4}$  alkyl,  $C_{2-4}$  alkynyl or cyano;

with the proviso that when  $p$  is 1 and  $Z$  is  $NH$ ,  $R^5$  cannot represent  $CH_3$ .

2. The compound of claim 1, wherein  $X$  is  $CR^1$  and  $Y$  is  $CR^2$ .

3. The compound of claim 1, wherein  $X$  is  $CR^1$  and  $Y$  is  $N$ .

4. The compound of claim 1, wherein  $R^2$  is hydrogen, halogen or  $C_{1-4}$  alkoxy.

5. The compound of claim 1, wherein  $R^2$  is hydrogen, fluoro or methoxy.

6. The compound of claim 1, wherein  $R^2$  is hydrogen or fluoro.

7. The compound of claim 1, wherein  $Z$  is  $NH$ ,  $NR^6$  or  $O$ .

8. The compound of claim 1, wherein  $Z$  is  $NH$  or  $O$ .

9. The compound of claim 1, wherein  $Z$  is  $NH$ .

10. The compound of claim 1, wherein  $p$  is 1, 2 or 3.

11. The compound of claim 1, wherein  $Ar$  does not carry any optional substituents.

12. The compound of claim 1, wherein  $Ar$  is furan or thiazole.

206070-2250E001

13. The compound of claim 1, wherein  $R^5$  is an aromatic heterocyclic or carbocyclic group optionally substituted by a  $C_{1-4}$  alkyl group.
- 5 14. The compound of claim 1, wherein  $R^5$  is pyridyl, phenyl, imidazolyl or N-methylimidazolyl.
15. The compound of claim 1, wherein  $R^5$  is  $C_{1-6}$  alkyl optionally substituted by one or more groups selected from halo, hydroxy,  $C_{1-4}$  alkoxy, nitrile,  $NH_2$  or  $NR^6R^7$ .
- 10 16. The compound of claim 1, wherein  $R^5$  is  $C_{1-6}$  alkyl optionally substituted by one or more groups selected from hydroxy,  $C_{1-4}$  alkoxy,  $NH_2$  or  $NR^6R^7$ , wherein  $R^6$  represents  $C_{1-4}$  alkyl.
- 15 17. The compound of claim 1, wherein  $R^5$  is unsubstituted  $C_{1-6}$  alkyl.
18. The compound of claim 1, wherein  $R^3$  is benzyloxy or fluorobenzyloxy.
19. The compound of claim 1, wherein  $R^4$  is chloro, bromo, or hydrogen.
- 20 20. The compound of claim 1, wherein  $R^3$  is benzyloxy or 3-fluorobenzyloxy and  $R^4$  is chloro or bromo.
- 25 21. The compound of claim 1, wherein Y is  $CR^2$ ,  $R^2$  is hydrogen, fluoro or methoxy; X is  $CR^1$ , Ar is unsubstituted furan or thiazole;  $R^3$  is benzyloxy or fluorobenzyloxy; and  $R^4$  is hydrogen, chloro or bromo.
- 30 22. The compound of claim 1, wherein X is  $CR^2$ ,  $R^2$  is hydrogen, fluoro or methoxy; Y is  $CR^1$ , Ar is unsubstituted furan or thiazole;  $R^3$  is benzyloxy or fluorobenzyloxy; and  $R^4$  is hydrogen, chloro or bromo.
23. The compound of claim 1, wherein Y is N; X is  $CR^1$ , Ar is unsubstituted furan or thiazole;  $R^3$  is benzyloxy or fluorobenzyloxy; and  $R^4$  is hydrogen, chloro or bromo.

24. The compound of claim 1, wherein Y is CR<sup>2</sup>, R<sup>2</sup> is hydrogen, fluoro or methoxy; X is CR<sup>1</sup>, Ar is unsubstituted furan or thiazole; R<sup>3</sup> is fluorobenzyloxy; and R<sup>4</sup> is chloro or bromo.

5 25. The compound of claim 1, wherein Y is N; X is CR<sup>1</sup>, Ar is unsubstituted furan or thiazole; R<sup>3</sup> is fluorobenzyloxy; and R<sup>4</sup> is chloro or bromo.

10 26. The compound of claim 1, wherein Y is CR<sup>2</sup>, R<sup>2</sup> is hydrogen, fluoro or methoxy; X is CR<sup>1</sup>, Ar is unsubstituted furan or thiazole; R<sup>3</sup> is benzyloxy or fluorobenzyloxy; R<sup>4</sup> is hydrogen, chloro or bromo; and R<sup>5</sup> is unsubstituted C<sub>1-6</sub> alkyl.

15 27. The compound of claim 1, wherein X is CR<sup>2</sup>, R<sup>2</sup> is hydrogen, fluoro or methoxy; Y is CR<sup>1</sup>, Ar is unsubstituted furan or thiazole; R<sup>3</sup> is benzyloxy or fluorobenzyloxy; R<sup>4</sup> is hydrogen, chloro or bromo; and R<sup>5</sup> is unsubstituted C<sub>1-6</sub> alkyl.

28. The compound of claim 1, wherein Y is N; X is CR<sup>1</sup>, Ar is unsubstituted furan or thiazole; R<sup>3</sup> is benzyloxy or fluorobenzyloxy; R<sup>4</sup> is hydrogen, chloro or bromo; and R<sup>5</sup> is unsubstituted C<sub>1-6</sub> alkyl.

20 29. The compound of claim 1, wherein Y is CR<sup>2</sup>, R<sup>2</sup> is hydrogen, fluoro or methoxy; X is CR<sup>1</sup>, Ar is unsubstituted furan or thiazole; R<sup>3</sup> is fluorobenzyloxy; R<sup>4</sup> is chloro or bromo; and R<sup>5</sup> is unsubstituted C<sub>1-6</sub> alkyl.

25 30. The compound of claim 1, wherein Y is N; X is CR<sup>1</sup>, Ar is unsubstituted furan or thiazole; R<sup>3</sup> is fluorobenzyloxy; R<sup>4</sup> is chloro or bromo; and R<sup>5</sup> is unsubstituted C<sub>1-6</sub> alkyl.

30 31. The compound of claim 1, wherein Y is CR<sup>2</sup>, R<sup>2</sup> is hydrogen, fluoro or methoxy; X is CR<sup>1</sup>, Ar is unsubstituted furan or thiazole; R<sup>3</sup> is benzyloxy or fluorobenzyloxy; R<sup>4</sup> is hydrogen, chloro or bromo; and R<sup>5</sup> is pyridine, imidazole, or phenyl.

32. The compound of claim 1, wherein X is CR<sup>2</sup>, R<sup>2</sup> is hydrogen, fluoro or methoxy; Y is CR<sup>1</sup>, Ar is unsubstituted furan or thiazole; R<sup>3</sup> is benzyloxy or

20030527-010902

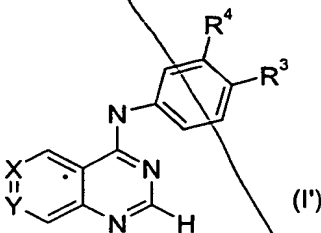
fluorobenzyloxy;  $R^4$  is hydrogen, chloro or bromo; and  $R^5$  is pyridine, imidazole, or phenyl.

33. The compound of claim 1, wherein Y is N; X is  $CR^1$ , Ar is unsubstituted furan or thiazole;  $R^3$  is benzyloxy or fluorobenzyloxy;  $R^4$  is hydrogen, chloro or bromo; and  $R^5$  is pyridine, imidazole, or phenyl.

34. The compound of claim 1, wherein Y is  $CR^2$ ,  $R^2$  is hydrogen, fluoro or methoxy; X is  $CR^1$ , Ar is unsubstituted furan or thiazole;  $R^3$  is fluorobenzyloxy;  $R^4$  is chloro or bromo; and  $R^5$  is pyridine, imidazole, or phenyl.

35. The compound of claim 1, wherein Y is N; X is  $CR^1$ , Ar is unsubstituted furan or thiazole;  $R^3$  is fluorobenzyloxy;  $R^4$  is chloro or bromo; and  $R^5$  is pyridine, imidazole, or phenyl.

36. A compound of any one of claims 1 to 35, wherein the compound is a compound of formula (I')



37. A compound of claim 1 selected from

- (4-(3-Fluorobenzyloxy)-3-chlorophenyl)-(6-(2-((2-phenylsulphonyl-ethylamino)-propyl)-furan-2-yl)-quinazolin-4-yl)-amine;  
 (4-(3-Fluorobenzyloxy)-3-chlorophenyl)-(6-(2-((2-(2-N-methylimidazolyl)-sulphonyl-ethylamino)-methyl)-furan-2-yl)-quinazolin-4-yl)-amine;  
 (4-(3-Fluorobenzyloxy)-phenyl)-(6-(2-((2-propanesulphonyl-ethylamino)methyl)-furan-2-yl)-pyrido[3,4-d]pyrimidin-4-yl)-amine;  
 (4-(3-Fluorobenzyloxy)-3-chlorophenyl)-(6-(2-((2-propanesulphonyl-ethylamino)-methyl)-furan-2-yl)-quinazolin-4-yl)-amine;  
 (4-Benzyloxy-3-chlorophenyl)-(6-(2-((2-methanesulphonyl-ethylamino) propyl)-furan-2-yl)-quinazolin-4-yl)-amine;

- (4-(3-Fluorobenzyloxy)-3-chlorophenyl)-(6-(2-((2-iso-propyl-sulphonyl-ethylamino)-propyl)-furan-2-yl)-quinazolin-4-yl)-amine;  
 (4-(3-Fluorobenzyloxy)-3-chlorophenyl)-(6-(2-((2-propanesulphonyl-ethylamino)-propyl)-furan-2-yl)-quinazolin-4-yl)-amine;  
 5 (4-(3-Fluorobenzyloxy)-3-chlorophenyl)-(6-(2-((2-methanesulphonyl-ethylamino)ethyl)-thiazol-4-yl)-quinazolin-4-yl)-amine;  
 4-(3-Fluorobenzyloxy)-3-chlorophenyl)-(6-(2-((2-methanesulphonyl-ethylamino)ethyl)-furan-2-yl)-quinazolin-4-yl)-amine;
- 10 and salts, solvates, or physiologically functional derivatives thereof.
38. A compound of claim 1 selected from
- 15 N-{3-chloro-4-[(3-fluorobenzyl)oxy]phenyl}-6-(5-[[2-(phenylsulfonyl)ethoxy]methyl]-2-furyl)-4-quinazolinamine;  
 (4-(3-Fluorobenzyloxy)-3-chlorophenyl)-(6-(2-((2-phenylsulphonyl-ethylamino)-methyl)-furan-2-yl)-quinazolin-4-yl)-amine;  
 (4-(3-Fluorobenzyloxy)-3-chlorophenyl)-(6-(2-((2-(2-pyridyl)-sulphonyl-ethylamino)-methyl)-furan-2-yl)-quinazolin-4-yl)-amine;  
 20 N-{3-chloro-4-[(3-fluorobenzyl)oxy]phenyl}-6-(5-[[2-(methylsulfonyl)ethoxy]methyl]-2-furyl)-4-quinazolinamine;  
 N-{3-chloro-4-[(3-fluorobenzyl)oxy]phenyl}-6-(5-[[2-(vinylsulfonyl)ethoxy]methyl]-2-furyl)-4-quinazolinamine;  
 25 2-[[5-(4-{3-chloro-4-[(3-fluorobenzyl)oxy]anilino}-6-quinazolinyl)-2-furyl]methyl][2-(methylsulfonyl)ethyl]amino}acetonitrile;  
 6-[5-({benzyl[2-(methylsulfonyl)ethyl]amino}methyl)-2-furyl]-N-{3-chloro-4-[(3-fluorobenzyl)oxy]phenyl}-4-quinazolinamine;  
 N-{3-chloro-4-[(3-fluorobenzyl)oxy]phenyl}-6-[5-({ethyl[2-methylsulfonyl]ethyl}amino}methyl)-2-furyl]-4-quinazolinamine;  
 30 N-{3-chloro-4-[(3-fluorobenzyl)oxy]phenyl}-6-(5-[[2-(methylsulfonyl)ethyl](propyl)amino]methyl)-2-furyl)-4-quinazolinamine;  
 (4-(3-Fluorobenzyloxy)-3-chlorophenyl)-(6-(2-((2-iso-propyl-sulphonyl-ethylamino)-methyl)-furan-2-yl)-quinazolin-4-yl)-amine;
- 35 and salts, solvates, or physiologically functional derivatives thereof.

- Sub A<sub>3</sub>  
 39. A pharmaceutical composition, comprising: a therapeutically effective amount of at least one compound as claimed in claims 1 to 38 and one or more pharmaceutically acceptable carriers, diluents or excipients.

Sub  
Py  
5 40. A method of treating a human or animal subject suffering from a disorder mediated by aberrant protein kinase activity, comprising administering to said mammal a therapeutically effective amount of at least one compound as claimed in claims 1 to 38.

41. The method of claim 40, wherein the disorder is cancer or psoriasis.

42. The method of claim 40, wherein two or more protein kinases selected from c-ERB-B2, c-ERB-B4, or EGFr, exhibit aberrant activity.

10 43. The method of claim 40, wherein c-ERB-B2 and EGFr exhibit aberrant activity,

15 44. Use of a compound as claimed in claims 1 to 38 in the preparation of a medicament for the treatment of a disorder mediated by aberrant protein kinase activity.

45. The use of claim 44, wherein the disorder is cancer or psoriasis.

20 46. The use of claim 44, wherein two or more protein kinases selected from c-ERB-B2, c-ERB-B4, or EGFr, exhibit aberrant activity.

47. The use of claim 44, wherein c-ERB-B2 and EGFr exhibit aberrant activity,

25 48. A compound as claimed in claims 1 to 38 for use in therapy.

205010" 22508001